

AN EVALUATION OF THE SURGICAL TREATMENT OF ANGINA PECTORIS*

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A critical appraisal of the different forms of surgical treatment of angina pectoris should properly include a detailed consideration of the theoretical aspects of each type of operation, as well as of the actual results obtained. The time at our disposal is so relatively limited that any discussion of the anatomical and physiological basis must be brief and quite inadequate. Those of you who wish a more comprehensive knowledge of this aspect of the problem may profitably read the excellent series of papers by those authors to whom I shall refer in a moment.

There are three types of operation that have been proposed and tried for the relief of anginal pain: (1) section or removal of a small or large part of the cervical sympathetic nerves or ganglia on one or both sides; (2) section of, or injection of alcohol into, the upper thoracic sympathetic ganglia or the corresponding dorsal nerve roots; and (3) total removal of the thyroid gland. I wish to discuss these briefly in that order.

In 1916 Jonnesco¹ of Bucharest first adopted a suggestion made by Francois-Franck seventeen years earlier. Franck was convinced on the basis of certain experimental observations and his review of cervical sympathectomy performed for various conditions, that these nerves served a sensory function and conveyed pain impulses from the heart to the central nervous system. Jonnesco performed widespread excision of the sympathetic nerves in the neck of a patient who had syphilitic aortitis and angina pectoris, and secured complete relief of pain. Despite this, the operation did not become popular, and in 1923 Coffey and Brown² of California suggested a much simpler procedure for the same pur-

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pose, namely, removal of a smaller portion of the sympathetic nerves or ganglia on one side only. Within the next five or six years a great many patients were subjected to this procedure or some modification of it, and when it became clear that unilateral resection was often ineffective, some surgeons returned to the more radical and extensive operation of Jonnesco which became known as cervico-thoracic sympathectomy, and consisted of the removal of all three cervical ganglia and the first dorsal or stellate ganglion on both sides. As will appear later, this bilateral operation was based upon beliefs now thought to be erroneous.

In 1933, White³ summarized the reported cases subjected to one or the other type of sympathectomy, and reported the results as follows: Of one hundred and eighteen cases subjected to upper cervical sympathectomies (Coffey and Brown), 48 per cent had a satisfactory result. Of sixty-six cases subjected to the complete cervico-thoracic sympathectomy (Jonnesco), 53 per cent had a satisfactory result. The operative mortality was from 7.5 to 12.5 for the simpler operation, and about 20 per cent for the complete Jonnesco procedure.

I am sure I need not remind you of the difficulty inherent in this method of appraising results. The degree of enthusiasm of the author may lead him to classify as highly satisfactory a result which impartial observers would regard as far less so, and it is a not uncommon experience, as Dr. Levy⁴ has pointed out, to find the tables and conclusions of certain authors at wide variance with the case reports upon which they are based. In other words, even if one accepts the author's own report of his cases, it becomes impossible in many instances to agree with his classification of results. Acknowledging this difficulty, it is interesting to find one of the more enthusiastic of the earlier advocates of sympathectomy speaking thus in 1933:⁵ "It seems to us that the results in all of the procedures enumerated and so frequently practised fail to give a sufficiently satisfactory percentage of good results to let us feel that we are on the right track in treating this disorder. . . . It is true also that

the risk of the major operation is something to be considered. We have convinced ourselves that the figures for the various procedures on the sympathetic apparatus in the treatment of angina pectoris are not sufficiently hopeful to justify continued minor perfections in the technique already at hand. Certainly the changes brought about are only of a quantitative measure, and complete relief has rarely been given. It would appear that the basic considerations must be somewhere faulty."

I believe it is correct to state that cervical sympathectomy has fallen into almost complete disuse because increasing experience indicated that the results did not justify the procedure. I have written to a number of those who were at one time interested in this form of treatment, and practically all who have replied indicate that they are no longer advocating it. Since there is now excellent reason for thinking that the operation was based upon incorrect beliefs, it seems to me unnecessary to consider it further.

In 1925, Mandl⁶ in Europe, and in 1926 Dr. George Swetlow⁷ of this city, reported groups of anginal patients who had been remarkably relieved of pain by the paravertebral injection of alcohol into the dorsal nerve roots on the left side. In these earlier reports the procedure was not standardized as to the number of nerves to be injected; in Swetlow's cases the decision depended in some measure upon the areas of hyperesthesia in the skin that could be discovered by careful protopathic and epicritic sensory tests; from the studies of Head and of Mackenzie, it was thought that these areas would indicate the dorsal root ganglia that were being irritated by the passage of pain impulses from the heart. In the eight patients first reported by Swetlow, alcohol was injected into from two to nine dorsal nerve roots; prompt and satisfactory relief from pain was secured in every instance. In a paper five years later, he reported a group of twenty-two patients, with relief in eighteen of them.

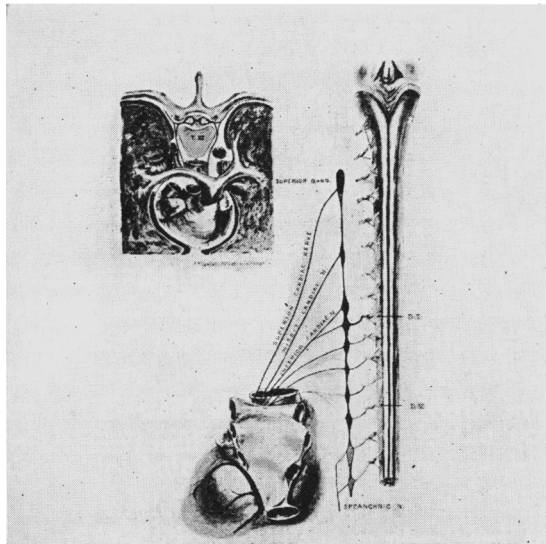
Between 1926 and 1930, observations of fundamental importance in this connection were reported by a number of

different observers^{8, 9, 10, 11}, who demonstrated the existence of postganglionic fibers leaving the upper two to four thoracic ganglia and running into the posterior cardiac plexus. These were demonstrated in laboratory animals and in man, by anatomical and physiological methods. If it could be shown that these fibers carried sensory or motor impulses which played an important part in the production of anginal pain, it would immediately become obvious why cervical sympathectomy had been unsuccessful, for no operation performed through the neck could sever these structures, and their persistence would account for the continuance of anginal pain after even complete cervical sympathectomy.

With this possibility in mind, James White of Boston and his collaborators³ performed a series of experiments upon dogs. As an indicator of the occurrence of pain, they employed the method of Sutton and Lueth,¹² passing a ligature about the left anterior coronary artery and leading it out through the wound, which was then closed. Brief traction upon this ligature would cause occlusion of the artery, and the resulting ischemia of the heart muscle invariably caused characteristic changes in the behavior of the animal, stiffening of the limbs, a marked increase in the rate and depth of respiration, and considerable restlessness. In twenty-one animals this was used as an index of the effectiveness of various neurosurgical operations for interrupting the pathways of cardiac pain, or of impulses thought to correspond with pain impulses in man. Their results may be summarized briefly as follows: Cardiac pain was not transmitted by the vagus nerves; bilateral section of these nerves did not alter the characteristic response of the animal to coronary arterial occlusion. If afferent impulses from the areas to which cardiac pain is usually referred were blocked by section of the upper intercostal nerves on both sides, pain was not prevented. Bilateral resection of the stellate ganglia might diminish, but did not block, all sensory stimuli from the heart; a distinct sensory response was obtained in five of six animals in which this test was made.

On the other hand, bilateral removal of the sympathetic ganglia from the stellate down through the fourth thoracic ganglion, or section of the upper five posterior dorsal nerve roots, appeared to interrupt all sensation from the heart. They showed that bilateral excision of the stellate ganglia did not completely destroy the motor pathways to the heart. The upper thoracic ganglia (below the stellate) send important motor as well as sensory fibers directly across the posterior mediastinum to the posterior cardiac plexus. If these are stimulated electrically, the heart rate may increase as much as 58 per cent.

These statements concerning the anatomical and physiological relationships of the heart and the sympathetic system will perhaps be clarified by reference to the illustration. This photograph is of a drawing in a paper by Dr.



James White which appeared in August, 1933.¹³ The heart and spinal cord are viewed from the back, and the position of the heart has been shifted to the left for purposes of illustration. The heavy black line represents the sympathetic trunk, beginning with the superior cervical ganglion and showing the successive ganglia down to the

fifth dorsal. The lines connecting these ganglia with the posterior cardiac plexus represent in order the superior, middle and inferior cardiac nerves running from the corresponding sympathetic ganglia, and below these the fibers mentioned as having been described between 1926 and 1930 by a number of different observers. These run directly across the posterior mediastinum and apparently carry both sensory and motor impulses. The middle and inferior cardiac nerves carry both afferent and efferent stimuli, but the superior cardiac nerve is thought to be purely motor. It is important to recognize that all of the cardiac fibers concerned in the conduction of pain impulses converge in the upper thoracic ganglia and then enter the spinal cord over the white communicant rami and the posterior roots. According to our present conceptions, there are no white communicant rami joining the upper cervical ganglia with the spinal cord, so that impulses travelling from the heart over the middle and inferior cardiac nerves must travel downward in the sympathetic chain and be transmitted through the four or five upper dorsal ganglia. It is clear from this diagram why even complete removal of the cervical sympathetic ganglia may fail to relieve anginal pain. Even if all three cervical ganglia are removed, there still remain these nerves running to the five upper dorsal ganglia which may convey pain impulses. These can be completely interrupted by blocking the ganglia, the rami or the spinal roots.

These anatomical and physiological premises have been tested in a total of forty cases at the Massachusetts General Hospital suffering from the severest forms of anginal pain. Thirty-six of these had alcohol injections into the dorsal nerve roots or ganglia, and four were subjected to surgical resection of the upper four thoracic ganglia. Of the total number, there was complete or almost complete improvement (90 to 100 per cent relief) in more than half, and marked improvement (estimated at 50 to 90 per cent relief) in another 25 per cent. There was slight improvement (estimated at 25 to 50 per cent) in 8 per cent, and failure, due to technical difficulties in placing the alcohol precisely, in

about 12 per cent. There was no operative mortality from the paravertebral alcohol injections, but White estimates that there will be an inevitable mortality of about 25 per cent from surgical resection of the upper four thoracic ganglia.

Dr. Robert Levy, whose excellent paper upon this subject in 1931⁴ led me to write him several weeks ago, has been kind enough to send me the following informal report upon the Presbyterian Hospital series of cases of alcohol injection for the relief of anginal pain. There have been about thirty cases in all; in approximately 40 per cent there has been a considerable measure of relief, varying from complete disappearance of pain to a reduction in the number and intensity of attacks. In another 30 per cent lesser degrees of improvement were noted, and in the remaining 30 per cent the procedure was classified as a failure. These figures are approximate, and represent Dr. Levy's impressions rather than a careful analysis of his cases. I would ask you to bear in mind that the differences in results at different clinics are not to be construed as invalidating the anatomical and physiological studies of White, but rather as indicating differences in experience and in technical skill. Several competent surgeons have told me, for example, that they are unable to perform the injection with any degree of success, and Dr. White tells me his technique is acceptable to himself only when he can perform injections on the average of about once a week.

Swetlow speaks of the relief in his patients as lasting for a number of months, but both White and Levy have found that there was no recurrence of pain in their patients who were relieved, and some of these have been followed for five or six years.

When we realize that the patients subjected to paravertebral alcohol injections have been selected purely on the basis of severity and frequency of pain, that they were critically ill, and that life was almost insupportable, these results are most impressive. There are, however, several objections that must be mentioned. The chief of these is the

appearance, in about one-half to two-thirds of the cases, of a severe alcoholic neuritis of the infiltrated intercostal nerves, leading to moderate or severe hyperesthesia and pain. This may last from several weeks to several months, and in a few cases is quite distressing. The second objection is the technical difficulty of injecting the alcohol with precision, since it has to be done blindly. The injection of 5 c.c. of alcohol results in an area of fibrosis about 1 cm. in diameter, and if this is to be effective, it must involve the exact area desired. In several reported instances, the alcohol has touched the pleura or has been injected into the pleural cavity and has led to transient pleurisy. In general, however, it must be regarded as a safe surgical procedure, without serious permanent complications, and without operative mortality.

There is one question which inevitably and quite properly comes to mind in this connection. Is it dangerous to abolish pain in these patients? Is anginal pain truly a warning, the removal of which will permit the patient to continue harmful exertion beyond the proper point and thus cause death? This question was vehemently debated in connection with the operation of cervical sympathectomy, but so far as I am aware, no clear evidence was ever brought forward in proof of the belief that patients would be worse without their warning pain. Similarly, I know of no evidence to indicate that alcohol injections have hastened death by permitting patients to indulge in excessive activity. Actually, the question is one that is very difficult, and perhaps impossible, to answer, for the patients who have been subjected to these procedures are precisely those to whom sudden death may come at any time. If they die suddenly some weeks or months after operation, who can assert with any confidence that the end has been hastened or postponed by the treatment? Actually, it is true to say that in most, if not in all, cases, there are substitution symptoms which serve as warnings just as effectively as did pain before its removal; such symptoms as a sense of emptiness in the epigastrium, oppression in the chest, or slight constriction of the throat.

I come now to the third and last of the surgical methods of treatment, namely, removal of the entire thyroid gland. I believe the largest experience with this method of treatment has been acquired by Levine and Cutler at the Peter Bent Brigham Hospital, and by Blumgart and his collaborators at the Beth Israel Hospital, in Boston. Most of you are doubtless familiar with their papers and with the slightly divergent views which they champion. Within the past two weeks I have had the privilege of discussing this matter at length with Doctors Blumgart, Davis and Riesenman at the Beth Israel Hospital, with Doctors Cutler and Levine at the Peter Bent Brigham Hospital, with Doctors Weiss and Faulkner at the Boston City Hospital, and with Doctors Paul White, Howard Sprague and James White at the Massachusetts General Hospital. While my brief remarks upon the subject are based largely upon published reports, they are doubtless colored by my recent discussions with these men and by my own experience with the method in New Haven.

There is general agreement that during or immediately after such operation, the majority of patients are relieved of anginal pain. According to Blumgart, this instant relief is due to section of or trauma to sympathetic nerves in close proximity to the thyroid gland, and pain will return when the nerves regain their function. According to Levine and Cutler, the immediate relief is due to an altered response of the heart to adrenalin, and they have shown that the response of the cat's denervated heart to adrenalin is altered by removal of the thyroid gland from such animals. Blumgart, however, has shown that if only one lobe of the thyroid be removed from a patient who has angina with bilateral radiation of pain, there is immediate relief of pain on the operated side only. It is difficult to believe that this unilateral relief could be due to altered sensitivity to adrenalin circulating in the blood stream. Furthermore, Blumgart has shown that the response of the heart rate and blood pressure to intravenous injections of dilute adrenalin in man are precisely the same after thyroidectomy as before, until the basal metabolic rate falls to very low levels, which

usually requires three or four weeks. It is his conception that the immediate relief is due to cutting of nerves, and the permanent relief is associated with the lessened demands upon the heart attendant upon the development of hypothyroidism. His views seem so logical, and the evidence supporting them seems so unequivocal, that one is tempted to agree with them wholly, but there are many questions still unanswered, and further experience alone will provide the solutions that we seek.

What results have been obtained? I believe it is impossible at present to make any fair or final answer. Unquestionably some patients have been completely relieved of pain, and a larger number have been greatly helped. There have been a considerable number of failures, and a small number of operative deaths. Some patients have been relieved of pain, only to suffer the severe discomforts of myxedema, while others oscillate back and forth between myxedema and angina, depending on the dose of thyroid extract administered. So far as actual figures are concerned, Blumgart¹⁴ reports that eight of twenty-five patients secured complete relief from pain lasting up to the time of publication of his paper, which was from three to eighteen months after operation. Five were improved, four had no relief, and six had recurrence of anginal pain after from three to nine months of complete relief. These figures in themselves seem to indicate that the physiological basis for the procedure is probably not fully understood. If relief of pain is actually due to lessened demands upon the heart associated with hypothyroidism, why should only eight of twenty-five patients secure lasting relief when hypothyroidism is produced? Why should six patients be completely relieved of pain, only to have it return six months later while the basal metabolism was still at a low level? Why do some patients secure relief from pain only when the metabolic rate falls to low levels, and have recurrences of pain if the metabolism is elevated even slightly, while others secure relief in a similar fashion and yet have no recurrences of pain even if the metabolism is raised to the pre-operative level by means of thyroid extract? The evidence

in some respects is not only confusing, but also contradictory, and if the reported observations are correct, there can be little question that the evidence is still far from complete. It is possible that Cutler is right in believing that thyroidectomy has influences upon the circulation other than, and independent of, those which can be measured in terms of the basal metabolism. Until further studies can be completed, it seems impossible to state dogmatically the full reasons for the benefit which occurs in about one-third of the cases.

Moreover, there are certain surgical hazards which cannot possibly be ignored. The chief of these are sudden death within a few hours of operation, postoperative pulmonary complications which may lead to death several days later, injury to the recurrent laryngeal nerve, and parathyroid insufficiency. Unless these patients are treated with extreme care, the operative and postoperative mortality is apt to be rather high.

It was natural to believe, when this operation was first proposed, that serious results might follow the deliberate induction of surgical myxedema. Among these were mentioned the so-called myxedema heart, in the sense of a causal condition precipitating circulatory failure or angina pectoris, mental changes similar to those often associated with spontaneous myxedema, rapid development of arteriosclerosis because of the high level of cholesterol in the blood serum associated with hypothyroidism, and the anemia which is so often a part of spontaneous myxedema. These possible developments have been kept clearly in mind by Blumgart, and a large number of patients have been carefully studied to see if these conditions would develop. Up to the present time there is no evidence that they have been important. Despite this, the potential and actual disadvantages of thyroidectomy are numerous, and there is complete agreement among all those with whom I have talked that a certain number of patients have been made worse by the operation, not with respect to pain, but with respect to other symptoms. The discomforts and crippling effects of myxedema are too numerous and serious to be ignored, and

the final state of some patients after operation is most pitiable. It seems pertinent to indicate that with the exception of the Beth Israel group, those with whom I have discussed the matter are far less enthusiastic today than they were a year ago.

These I believe to be the chief matters for consideration in attempting to appraise the value of these surgical procedures individually and with respect to each other. I have already indicated that there is now a general belief that operations upon the cervical sympathetic trunk are physiologically unsound and not warranted in the light of present knowledge.

A comparison of the other two methods may be attempted, but any conclusions now reached may well be modified by future experience. It should be kept clearly in mind that the two have quite different aims; the injection of alcohol has as its objective the destruction of nerves which convey pain; in a sense it aims at producing permanent local anesthesia. Thyroidectomy, on the other hand, theoretically aims at removing the discrepancy between the demands of the body and the ability of the heart to meet those demands. Anginal pain is thought to be the expression of this discrepancy, and since the ability of the heart cannot be increased in terms of the coronary blood flow, it would seem logical to decrease the demands of the body, and thus remove the cause of the pain. There is no apparent reason for questioning the physiological basis for the first procedure; there are several reasons for questioning the current explanations of the relief afforded by thyroidectomy. Until we know beyond all question exactly what thyroidectomy does, the only comparison that is valid is of the results achieved by the two methods, both good and bad, and of the obvious advantages and disadvantages of each. Accepting the reported results as published or as reported verbally to me, the percentage of relief following alcohol injections is higher than that following thyroidectomy, at least in the Boston groups. Further advantages of this procedure are the absence of operative mortality, the absence of any per-

manent ill-effects, the short period of hospitalization (usually three or four days, as compared with several weeks for thyroidectomy), and the possibility that other methods may be tried in case of failure, without the patient's condition having been altered for the worse. The disadvantages have already been indicated; they are chiefly three: the technical difficulty of injecting the alcohol accurately, the neuritis that often follows it, and the fact that relief is strictly limited to the side on which injection is performed. . . . In favor of thyroidectomy one may say that it affords great or moderate relief in one-third to one-half of the patients, including those who have bilateral radiation of pain. So far as I know, this is its only actual advantage as compared with the other procedure. The disadvantages are numerous and have been mentioned briefly; they include operative and postoperative death, recurrent laryngeal nerve paralysis, parathyroid insufficiency, myxedema, and the disturbing fact that we are still uncertain of the physiological basis for the operation.

A final question may profitably be asked. Is there a place for either or both of these therapeutic procedures in the treatment of anginal heart failure? In my opinion there is most certainly a place for alcohol injections. I believe the present evidence indicates that thyroidectomy will also find a permanent place in the treatment of angina, although I share the prevailing belief that at present it should be reserved for those patients in whom pain makes life intolerable or prevents the earning of a livelihood. The criteria for the selection of suitable patients are not yet sufficiently known, and it is possible that it will ultimately be reserved for a few severely ill patients who have bilateral radiation of pain, who have hyperthyroidism in addition to angina, or who have failed to respond to alcohol injections. The injection of alcohol would seem to me the method of first choice because of the high incidence of success and its freedom from the distressing conditions which may follow removal of the thyroid gland.

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DISCUSSIONS

DR. ALEXANDER LAMBERT: That was an extremely interesting and instructive summary that Dr. Marvin just finished; and one which I followed with great pleasure. It was on a subject in which I had long been interested, and I had followed closely the literature as it had appeared. As he summed up the thyroid operation for angina pectoris, it reminded me of the old Greek aphorism that was said of opium, "opium cures a disease, and produces a disease." I think this surgical procedure does the same. The elder Kocher, years ago, found that total ablation of the thyroid left a condition in which the several forms of thyroid medication could not prevent myxedema, and with it the myxedematous heart.